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Bukalasa, Joseph S; Brunekreef, Bert; Koppelman, Gerard H; Vonk, Judith M; Gehring, Ulrike

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Use of cleaning agents at home and respiratory and allergic symptoms in adolescents: The PIAMA birth cohort study

Joseph S. Bukalasa[a], Bert Brunekreef[a,b], Gerard H. Koppelman[c,d], Judith M. Vonk[d,e], Ulrike Gehring[a,*]

[a] Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands
[b] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands
[c] University of Groningen, University Medical Center Groningen, Beatrix Children's Hospital, Department of Pediatric Pulmonology and Pediatric Allergology, Groningen, the Netherlands
[d] University of Groningen, University Medical Center Groningen, Groningen Research Institute for Asthma and COPD (GRIAC), Groningen, the Netherlands
[e] University of Groningen, University Medical Center Groningen, Department of Epidemiology, Groningen, the Netherlands

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ABSTRACT

Background: It has been suggested that adults who use cleaning agents in their homes have a higher risk of asthma and allergic symptoms. The associations of asthma and allergic symptoms with household use of cleaning agents in adolescents have not been investigated yet.

Objectives: To examine the associations of household cleaning agents use with the prevalence of asthma, rhinitis and eczema in adolescents.

Methods: In this cross-sectional analysis, we included participants of the PIAMA birth cohort study with data on household use of 10 types of cleaning agents and information on asthma, rhinitis and/or eczema from parent-completed questionnaires at age 14 ($N = 2333$). For the cleaning agents, we developed a composite score ranging from 0 (no exposure) to 30 points (household use on 4–7 days per week for all 10 types of cleaning agents). Logistic regression was used to analyse associations between household cleaning agents use (composite score and specific cleaning agents) and outcomes, adjusting for potential confounders.

Results: Seven, 13 and 11% of the participants had asthma, rhinitis and eczema, respectively, at age 14. The composite score for household use of cleaning agents was not associated with asthma, rhinitis and eczema. For instance, adjusted odds ratios (95% confidence interval) for the prevalence of asthma, rhinitis and eczema comparing those with the highest use of cleaning agents (≥10 points) to those with never/seldom use (0–4 points) were 0.95 (0.56, 1.63), 1.23 (0.82, 1.82) and 0.95 (0.56, 1.63), respectively. For individual cleaning agents, we only found the use of ammonia to be significantly associated with a lower risk of rhinitis [0.60, (0.44, 0.82)].

Conclusions: There was no indication of an increased prevalence of asthma, rhinitis or eczema among adolescents living in households within the highest category of cleaning agents use.

1. Introduction

Cleaning agents are used in households to enhance domestic cleanliness and hygiene. Cleaning agents consist of a wide range of active ingredients (Lynch, 2000; Franzblau and Sahakian, 2003; Deschamps et al., 1994; Gorguner et al., 2004). Many of these active ingredients are risk factors for skin and lung diseases such as eczema and asthma in children and adults (Weinmann et al., 2017; Zock et al., 2009; Casas et al., 2013a; Krauss-Etschmann et al., 2009). The possible mechanisms underlying the adverse associations of cleaning agents use with asthma, rhinitis and eczema include irritation of mucous membranes and skin, a potential reduction of the epithelial barrier function, and occasionally, a sensitizing potential of the cleaning agents (Quirce and Barranco, 2010).

Most of the published epidemiological studies on the effects of cleaning agents use on asthma (Kogevinas et al., 1999; Medina-Ramon et al., 2003; Medina-Ramon et al., 2005; Zock et al., 2010; Arif et al., 2003) focused on the professional user. These studies found a significantly higher risk of asthma and lower respiratory tract infections in adult professional users of cleaning agents. Moreover, some studies also

* Corresponding author at: Utrecht University, Institute for Risk Assessment Sciences, P.O. Box 80178, 3508 TD Utrecht, the Netherlands.
E-mail address: u.gehring@uu.nl (U. Gehring).

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suggested that non-professional users of cleaning agents may have a higher risk of asthma, wheeze and lower-airway symptoms (Matulonga et al., 2016; Weinmann et al., 2017; Bedard et al., 2014; Zock et al., 2007). These associations maybe restricted to adults involved in cleaning activities in the home, subjecting themselves to a high level of exposure to cleaning agents. For instance, an epidemiological study found that weekly household use of cleaning sprays was associated with an increased risk of current asthma in elderly women involved in cleaning activities in their homes, but not in elderly women who had their homes cleaned by a household help (Bedard et al., 2014). Some studies have suggested that household chemical use including cleaning agents during pregnancy increases the risk of early childhood wheezing (Henderson et al., 2008; Sherriff et al., 2005; Casas et al., 2013a; Herr et al., 2012). Moreover, children living in a household with regular use of cleaning agents have been found to have a higher risk of rhinitis (Liu et al., 2016). The evidence from epidemiological studies regarding the association of cleaning agents use with respiratory and allergic symptoms in children, however, is inconsistent as another study found that children living in a house frequently cleaned with chlorine bleach had a lower risk of developing asthma and eczema (Nickmilder et al., 2007).

Although children do not use cleaning agents themselves, it is of interest to investigate associations in children because they are potentially exposed to cleaning agents used in their homes and they maybe more susceptible to the adverse effects than adults as their organs and immune system are still developing.

To our knowledge, no studies so far have investigated the associations of cleaning agents used in a household with respiratory and allergic symptoms in adolescents. We examined the associations of cleaning agents use in households with the prevalence of asthma, rhinitis and eczema symptoms in adolescents participating in the PIAMA birth cohort study at age 14 years.

2. Methodology

2.1. Study design and population

The PIAMA (Prevention and Incidence of Asthma and Mite Allergy) study is a prospective Dutch birth cohort study. The baseline study population consisted of 3963 newborns from the northern, middle and western parts of The Netherlands, who were born in 1996 and 1997 (Wijga et al., 2014). The PIAMA study has been designed to study the influence of lifestyle and environmental factors on the development of asthma and allergies in children. Questionnaires were administered to the parents during pregnancy, at the child's ages of 3 months and 1 year, and then annually until the age of 8 years. When the children were 11, 14, and 17 years old, both parents and children completed questionnaires. In this study, we performed a cross-sectional analysis using data from the questionnaires completed by the parents when the children were about 14 years old. The questionnaire administered at that age was the only one in which we included detailed questions on the use of household cleaning agents. The questions on use of cleaning agents were adapted from the questions used within the European Respiratory Health Survey (ECRHS) (Zock et al., 2009) and have been used also by other birth cohorts (Casas et al., 2013b).

2.2. Health outcomes

Asthma in the last 12 months was defined based on the presence of at least 2 out of 3 criteria (doctor-diagnosed asthma ever, wheezing during the past 12 months, and prescribed asthma medication during the past 12 months), a definition developed by a panel of experts within the MeDALL consortium (Pinart et al., 2014). Rhinitis in the last 12 months and eczema in last the 12 months were included as additional health outcomes. Rhinitis was defined according to MeDALL as sneezing or a runny/blocked nose without having a cold in the last 12 months that was accompanied by itchy, watering eyes. Atopic eczema was defined as an itchy rash that was coming and going in the last 12 months at one or more of the following locations: in the folds of the elbows, behind the knees, in front of the ankles, around the ears or eyes.

2.3. Use of cleaning agents at home

When the participants were 14 years old, we asked their parents about the use of the following cleaning agents in the home in the past 12 months (“never”, “less than once a week”, “1–3 times per week” and “4–7 times per week”): bleach/chlorine, ammonia, acids and (liquid) decalcifiers, solvents (including stain removers); furniture sprays, glass cleaning sprays (for windows and mirrors), fat removing sprays (including oven cleaning sprays), floor or furniture polish (no sprays), non-electric air fresheners, and automatic (electric) or plug-in air fresheners.

We used the questionnaire reported use of specific agents to define exposure to specific cleaning agents. For most of the individual cleaning agents, we combined some of the answering categories to have sufficient numbers (at least 10% of the subjects) in all exposure categories. For instance, answering categories “1–3 times a week” and “4–7 times a week” were merged for bleach/chlorine, acids and (liquid) decalcifiers, glass cleaning sprays, and fat removing sprays (including oven cleaning sprays). “Less than once a week”, “1–3 times a week” and “4–7 times a week” were combined into one category (“ever”) for ammonia and solvents (including stain removers), furniture sprays, floor or furniture polish (no sprays), and use of automatic (electric) or plug-in air fresheners.

In addition, we developed a composite score based on the use of the ten cleaning agents described above. This approach has been previously used by others (Sherriff et al., 2005; Weinmann et al., 2017; Liu et al., 2016; Mehta et al., 2012; Bedard et al., 2014). The score was developed to take into account that multiple cleaning agents may be used in the homes of the participants. For calculation of the score, first, points were assigned based on the reported use of cleaning agents as follows: never = 0 point, less than once a week = 1 point, 1–3 times per week = 2 points, 4–7 times per week = 3 points. Then, the points were summed up to produce a composite score which ranged from 0 (no use at all of any agent) to 30 (use on 4–7 days per week of all types of cleaning agents).

2.4. Potential confounding variables

We considered a number of potential confounding variables that we defined based on parental questionnaire reports: sex of the participant (male or female), smoking in the participant's home (yes or no), furry pets at home (cat, dog and/or rodent; yes or no), parental education (defined as the maximum of the mother's and the father's educational level and categorized as low (primary school, lower vocational, or lower secondary education), intermediate (intermediate vocational education or intermediate/higher secondary education) or high (higher vocational education and university)), damp stains/mould spots in the participant's bedroom and/or living room (yes or no), maternal and paternal allergy (yes or no), use of gas for cooking (yes or no), parental country of birth (both parents born in the Netherlands, yes or no), and active smoking of the participant. In addition, we considered estimated levels of traffic-related air pollution (annual average of nitrogen dioxide (NO_2)) at the participant's home address at the time of the outcome assessment (continuous) as a potential confounder as NO_2 has been found to be associated with asthma in earlier analyses within our cohort (Gehring et al., 2015). NO_2 levels were estimated by a land-use regression model developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE) project (Beelen et al., 2013). These potential confounding variables were selected because they have been identified in previous studies (Weinmann et al., 2017; Herr et al., 2012; Nickmilder et al., 2007; Krauss-Etschmann et al., 2009; Asher et al.,

1995) as determinants of the outcomes of interest (asthma, rhinitis and eczema).

2.5. Statistical analysis

For demographic variables, we performed descriptive statistical analyses calculating absolute numbers (n) and percentages (%) for categorical variables and means with standard deviations (SD) for continuous variables.

The composite score was categorized into four categories using quartiles as cut-offs: 'never/seldom' (0–4 points), 'low' (5–7 points), 'medium' (8–9 points) and 'high' (10 or more points).

We assessed associations of the composite score (categorical and continuous) and the use of specific cleaning agents with the prevalence asthma, rhinitis and eczema by logistic regression without and with adjustment for potential confounders and calculated odds ratios (ORs) with 95% confidence intervals (CIs).

As a sensitivity analysis, we assessed the associations of the use of cleaning agents with the prevalence of asthma, rhinitis, and eczema in the subset of participants that was reported to be sometimes or mostly present during cleaning activities.

We used Wald tests to determine the statistical significance of the relationships of cleaning agents use with prevalence asthma, rhinitis, and eczema. Statistical significance was defined as a p-value < 0.05. Statistical analyses were performed using SAS version 9.4.

3. Results

Approximately half of the study participants were male and for 92% of the participants both parents were born in the Netherlands (Table 1). The prevalence of asthma, rhinitis and eczema among the study participants were 7%, 13% and 11%, respectively (Table 1). The mean (standard deviation) of the composite score of cleaning agent use was 7.3 (3.3).

Tables 2 and S1 present the frequency distributions of parental-reported use of individual cleaning products after and before combining answering categories, respectively. The crosstables of individual cleaning product use with asthma, rhinitis, and eczema are presented in Table S2.

No statistically significant associations were observed between the composite score (categorical and continuous) and the prevalence of asthma, rhinitis and eczema (Table 3). For instance, the adjusted odds ratio (95% confidence interval) for the high vs. the never/low exposure category was 0.95 (0.56, 1.63) for asthma, 1.23 (0.83, 1.82) for rhinitis, and 0.95 (0.56, 1.63) for eczema, respectively (Table 3).When we investigated the associations of the use of individual cleaning products in the participants' homes with the prevalence of asthma, rhinitis and eczema in the adolescents, we did not find a higher prevalence among those living in homes where the cleaning products were used; on the contrary, the prevalence of rhinitis was found to be lower among study participants living in homes where ammonia was used as a cleaning product [adj. OR (95% CI) ever vs never 0.60 (0.44, 0.82), Fig. 1 and Table S3].

The results of the sensitivity analysis among the subset of 988 study participants, who were sometimes or mostly present indoors when the cleaning activities were conducted provided no evidence for an association of the composite score (continuous and categorical) with the prevalence of asthma, rhinitis and eczema (Table 4).

4. Discussion

This paper describes the associations of household use of cleaning agents with the prevalence of asthma, rhinitis and eczema at age 14 in participants of a Dutch prospective birth cohort study. The findings of this study suggest that the use of cleaning agents in the household, including cleaning products in spray form that may stay longer in the air and therefore pose a specific risk for asthma and allergic symptoms, is not associated with higher risks of asthma, rhinitis and eczema in this population.

Table 1
Distribution of covariates, health outcomes and composite exposure score in the study population at age 14 years (N = 2333).

Covariates		
Male sex, n/N [%]	1182/2333	[51]
Smoking in the child's home, n/N [%]	256/2333	[11]
Pets at home (cat, dog and/or rodent), n/N [%]	1389/2330	[60]
Damp stains/mould spots in child's bedroom and/or living room, n/N [%]	188/2329	[8]
Gas cooking, n/N [%]	1790/2331	[77]
Parental education, n/N [%]		
Low	231/2328	[10]
Intermediate	802/2328	[34]
High	1295/2328	[56]
Maternal and paternal allergy, n/N [%]		
Allergic father	730/2332	[31]
Allergic mother	681/2333	[29]
Both parents born in the Netherlands, n/N [%]	2093/2286	[92]
Active smoker, n/N [%]	102/2333	[4]
Traffic-related air pollution (NO_2) at the home address, mean (SD) [n]	22.6 (6.5)	[2320]
Health outcomes		
Asthma, n/N [%]	161/2329	[7]
Rhinitis, n/N [%]	301/2330	[13]
Eczema, n/N [%]	251/2329	[11]
Exposure to cleaning agents		
Composite score (categorical), n/N [%]		
Never/seldom (score 0–4 points)	469/2323	[20]
Low (score 5–7 points)	816/2323	[35]
Medium (score 8–9 points)	482/2323	[21]
High (score 10 or more points)	556/2323	[24]
Composite score as continuous variable, mean (SD) [n]	7.3 (3.3)	[2323]
Participants were present during cleaning activities, n/N [%]		
Nearly never/mostly not	344/2332	[58]
Sometimes/mostly yes	988/2332	[42]

In reviewing the relevant literature (a summary of that literature is provided in Table S4), we found that the reported associations between cleaning agent use in the household and asthma, rhinitis and eczema in children are inconsistent.

Herr et al. found no indication of a higher risk of mild or severe wheeze in children with an average age of 19 months when their parents used cleaning sprays (Herr et al., 2012). Another study reported no association between the use of cleaning agents during and after pregnancy and the risk of wheezing in children during the first year of life (Casas et al., 2013a).

To the best of our knowledge, there is only one study, which involved participants of similar age (although somewhat older, aged 19–24 years) as the current study participants. That study found that cleaning disinfectant use was associated with a higher risk of incident asthma in young adults (Weinmann et al., 2017). The fact that this study has found an association while no associations were found in other studies including ours might be at least partially explained by a higher active involvement in household cleaning in early adulthood than in childhood and adolescence. Also, Weinmann et al. included both, occupational and residential exposures to disinfectants and they were not able to disentangle the effects of occupational exposure from the effects of residential exposure. Therefore, the study by Weinmann et al. is not directly comparable with our study as a) occupational exposure has not been included in our study and in addition, occupational exposure is unlikely in our study among 14-year olds living in the Netherlands, and b) occupational exposures are likely higher than residential exposures. In addition, the same study found no association between the use of cleaning sprays and risk of asthma and wheeze in young adults (Weinmann et al., 2017).

Also, one study found that children of women with a higher

Table 2
Frequency distribution of use of cleaning agents in the household in the past 12 months in the study population at age 14 years (after combining of some of the answering categories, N = 2333).

Agent used	n/N	%
Bleach/chlorine		
Never	367/2333	16
Less than once a week	936/2333	40
1–3 times a week/4–7 times a week	1030/2333	44
Ammonia		
Never	1649/2328	71
Ever	679/2328	29
Acids and (liquid) decalcifiers		
Never	460/2333	20
Less than once a week	1290/2333	55
1–7 times a week	583/2333	25
Solvents (including stain removers)		
Never	1078/2332	46
Ever	1254/2332	54
Furniture spray		
Never	2018/2333	87
Ever	315/2333	13
Glass cleaning spray		
Never	752/2331	32
Less than once a week	990/2331	42
1–7 times a week	589/2331	25
Fat removing spray (also oven cleaning spray)		
Never	859/2332	37
Less than once a week	1037/2332	44
1–7 times a week	436/2332	19
Floor/furniture polisher (no spray)		
Never	1470/2331	63
Ever	861/2331	37
Air freshener (non-electric)		
Never	909/2331	39
Less than once a week	379/2331	16
1–3 times a week	380/2331	16
4–7 times a week	663/2331	28
Automatic (electric) or plug-in air freshener		
Never	2049/2332	88
Ever	283/2332	12

household chemical exposure (composite score, including cleaning agents and insecticides) during pregnancy had a higher risk of persistent wheeze during the first 42 months of life (Sherriff et al., 2005), and early-onset persistent wheeze and intermediate-onset transient wheeze at age 7 years (Henderson et al., 2008). As we did not collect data on the use of cleaning agents during pregnancy, we cannot directly compare those findings with ours.

A study in elderly women with an average age of 68 years found a significant association between weekly use of at least one cleaning spray and current asthma in women without household help, but not in women with a household help (Bedard et al., 2014). This suggests that active involvement in cleaning activities might be necessary to increase the risk of asthma. We do not have data on active involvement in cleaning activities in the PIAMA study, but active involvement in cleaning activities is likely not very common at the age studied, which may explain the lack of association in the present study. However, we cannot rule out that the lack of association in the current study could be due to a true non-effect of cleaning agents use in relation with asthma, rhinitis and eczema among adolescents.

The current study found that the use of ammonia was associated with a lower risk of rhinitis in our study participants. Currently, evidence on the association of cleaning agents use with the risk of rhinitis in children is limited (a summary of that literature is provided in Table S4). One study reported that cleaning agents use in the household was associated with a higher risk of rhinitis in children aged 10 years (Liu et al., 2016). Exposure in that study was defined as the total chemical burden (TCB) to 14 different types of chemicals including cleaning agents and insecticides and the fact that the association estimates were significant for the 3rd tertile, but not the 2nd tertile versus the 1st tertile suggest that the increase in risk is limited to the group with the highest exposure. That study did not only involve study participants somewhat younger than the participants of our study, but also cleaning agents use might be different from the present study. Also, the use of insecticides was included in the TCB score in addition to cleaning agents in that study, but not in ours. This may explain the discrepancy between the findings of that study and our study. Moreover, we cannot rule out that the association between ammonia use and rhinitis in our study is a chance finding as many associations were tested. Unfortunately, we lack more detailed data on use of ammonia cleaning products and statistical power to explore this in more detail. Therefore, this finding should be interpreted with caution.

Our findings for eczema are consistent with the findings of another study which also found no indication of an increase in the risk of allergic dermatitis in relation to the household use of cleaning agents in children with an average age of 10 years (Liu et al., 2018). In another study, however, children who lived in a household where disinfectants were used had a higher risk of atopic eczema and rash ever at age

Table 3
Unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for associations of exposure to cleaning agents as a composite score (as a categorical and continuous variable) with asthma, rhinitis and eczema at age 14 years.

Composite score	Asthma		Rhinitis		Eczema	
	N = 2319	*N* = 2249	*N* = 2321	*N* = 2250	N = 2319	N = 2249
	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[a]
Categorical						
Never/seldom (0–4 points)	Ref	Ref	Ref	Ref	Ref	Ref
Low (5–7 points)	1.10 (0.70, 1.74)	0.99 (0.61, 1.60)	1.16 (0.82, 1.64)	1.16 (0.81, 1.66)	1.24 (0.87, 1.78)	0.99 (0.61, 1.60)
Medium (8–9 points)	1.32 (0.81, 2.17)	1.27 (0.76, 2.12)	0.97 (0.66, 1.44)	0.97 (0.64, 1.46)	1.06 (0.70, 1.60)	1.27 (0.76, 2.12)
High (10 or more points)	0.96 (0.58, 1.59)	0.95 (0.56, 1.63)	1.17 (0.81, 1.69)	1.23 (0.83, 1.82)	0.78 (0.51, 1.19)	0.95 (0.56, 1.63)
Continuous (per 1 point increase)	1.00 (0.95, 1.05)	1.01 (0.95, 1.06)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)	0.97 (0.93, 1.01)	1.01 (0.95, 1.06)

[a] Adjusted for sex of the child, smoking in the child's home at age 14, active smoking of the participant, parental education, pets at home at age 14, maternal and paternal allergy, both parents Dutch nationality, gas cooking, damp/mould spots in the child's bedroom and/or living room, and traffic-related air pollution (NO_2) at age 14.

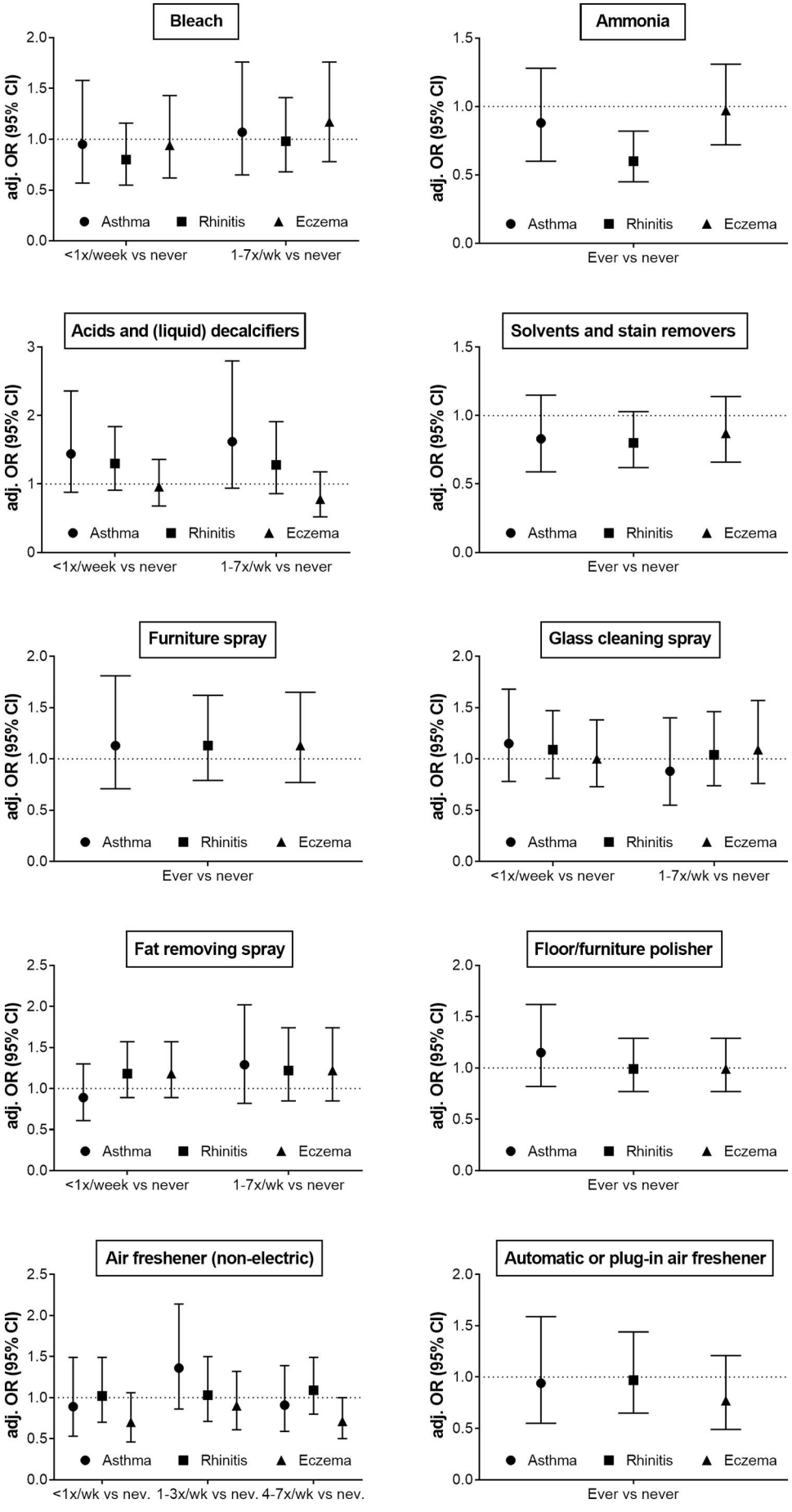

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Fig. 1. Adjusted[a] odds ratios (OR) with 95% confidence intervals (CI) for the associations of exposure to cleaning agents with asthma, rhinitis and eczema at age 14 years.
[a]Adjusted for sex of the child, smoking in the child's home at age 14, active smoking of the participant, parental education, pets at home at age 14, maternal and paternal allergy, both parents Dutch nationality, gas cooking, damp/mould spots in the child's bedroom and/or living room, and traffic-related air pollution (NO_2) at age 14.

4 years (Krauss-Etschmann et al., 2009). We did not investigate specifically the association between allergic dermatitis or atopic eczema and cleaning agents use, but most eczema in children is allergic (Krauss-Etschmann et al., 2009). The study by Krauss-Etschmann et al., however, is not directly comparable with our study because of the differences in the timing of the exposure (prenatal versus postnatal) as well as the age of the study participants. Also, younger children may be more likely to be exposed to the cleaning agents used as they spend more time at home compared to adolescents.

The lack of association with cleaning agents use in the household might be explained by the fact that most of the adolescents at age 14 in the Netherlands are not directly involved in cleaning activities and that they therefore, are likely exposed to low levels of cleaning agents. Moreover, many of our study participants were not present during the cleaning activities. However, a sensitivity analysis in the subsample of our study population that was sometimes or mostly present during cleaning activities confirmed the lack of association that was observed in the main analysis.

Previous studies and our study have only focused on the self-reported cleaning agents use and failed to address associations of individual chemical constituents present in cleaning agents with the risk of respiratory and allergic symptoms. We would suggest research that would look at the associations of the chemical constituents present in cleaning agents with a higher risk of respiratory and allergic symptoms in adolescents as this will provide an understanding of the associations of each chemical constituents present in cleaning agents used with the risk of asthma and allergic diseases.

This work was conducted in the Netherlands within the Dutch PIAMA birth cohort study. The participants were recruited from the general population as described previously (Wijga et al., 2014), to represent the general Dutch population of all children living in the Netherlands. However, children of highly educated parents were overrepresented and children of parents from non-western countries were underrepresented. There is currently no evidence for an increased or decreased susceptibility to effects of cleaning agents in children of highly educated parents or children of parents from non-western countries. Therefore, we think that the overrepresentation of children of highly educated and Dutch parents likely does not affect the generalisability of our study findings to the general population of all adolescents living in the Netherlands.

5. Conclusion

There was no indication of an increase in prevalence of asthma, rhinitis or eczema among adolescents living in households within the highest category of cleaning agents use.

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Conflict of interest statement

None of the authors declares an actual or potential conflict of interest.

Table 4
Unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for associations of exposure to cleaning agents as a composite score (categorical and continuous variable) with asthma, rhinitis and eczema at age 14 years for the subset of participants who were mostly and sometimes present in home when cleaning activities were conducted.

Composite score	Asthma		Rhinitis		Eczema	
	N = 982	*N* = 957	*N* = 985	*N* = 959	*N* = 984	N = 957
	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[a]
Categorical						
Never/seldom (0–4 points)	Ref	Ref	Ref	Ref	Ref	Ref
Low (5–7 points)	0.94 (0.43, 2.08)	0.91 (0.39, 2.14)	1.70 (0.86, 3.35)	2.14 (1.04, 4.41)	1.56 (0.81, 3.03)	0.91 (0.39, 2.14)
Medium (8–9 points)	1.08 (0.47, 2.48)	0.99 (0.41, 2.40)	1.43 (0.69, 2.97)	1.43 (0.65, 3.10)	1.30 (0.64, 2.66)	0.99 (0.41, 2.40)
High (10 or more points)	0.83 (0.37, 1.84)	0.91 (0.38, 2.17)	1.67 (0.85, 3.27)	1.95 (0.94, 4.01)	0.96 (0.48, 1.92)	0.91 (0.38, 2.17)
Continuous (per 1 point increase)	0.99 (0.92, 1.07)	1.01 (0.93, 1.10)	1.03 (0.97, 1.09)	1.03 (0.97, 1.09)	1.00 (0.94, 1.06)	1.01 (0.93, 1.10)

[a] Adjusted for sex of the child, smoking in the child's home at age 14, active smoking, parental education, pets at home at age 14, maternal and paternal atopy, both parents Dutch nationality, gas cooking, damp/mould spots in the child's bedroom and/or living room, and traffic-related air pollution (NO_2) at age 14.

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Appendix A. Supplementary tables

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.03.049.

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